SUPPORT FOR THE AMENDMENTS

The amendment to the specification merely corrects the priority claim, and thus does not constitute new matter. The amendments to the claims are fully supported by the specification. For example, the amendments to claim 13 are supported on page 12 lines 1-31 combined with page 19 lines 3-13. Thus, these amendments do not constitute new matter. Similarly, new claims 28-31 are supported, for example, on page 11 lines 22-24 and page 13 line 25 to page 14 line 15. Therefore, the new claims do not constitute new matter.

Remarks

1. Priority claim

The applicants have amended the specification to correct the priority claim. The mistake in the preceding priority claim was unintentional and any delay in correcting the priority claim was also unintentional. The applicants note that the instant application was filed on November 22, 2000, and is thus not subject to the limits on the time period for making priority claims under 37 CFR 1.78(a)(2) and (a)(5).

2. Claim objections

The patent office objected to claim 14 based on a typographical error in line 2. The applicants have amended the claim to correct the error, and note that this amendment does not in any way narrow the scope of the claim.

3. Claim rejections under 35 USC 112, second paragraph

(a) The patent office rejected claim 20 as being indefinite under 35 USC 112 second paragraph, based on the assertion that the term "field" is unclear as to what its relationship is to fluorescence imaging. The applicants traverse this rejection, but have in any event canceled the claim, thus obviating the rejection.

(b) The patent office rejected claim 27 as being indefinite under 35 USC 112 second paragraph, based on the assertion that the term "chemical environment" is indefinite. The applicants traverse this rejection, but have in any event canceled the claim, thus obviating the rejection.

(c) The patent office rejected claim 27 as being indefinite under 35 USC 112 second paragraph, based on the assertion that the use of "one or more of the following" is indefinite because the list of possibilities uses the term "and." The applicants traverse this rejection, but have in any event canceled the claim, thus obviating the rejection.

3. Claim rejections under 35 USC 103

(a) The patent office rejected claims 13-20 and 26 under 35 USC 103(a) as being obvious over US 5,869,238 ("Morrison") in view of US 6,210,910 ("Walt"). Specifically, the patent office asserts that Morrison teaches using fluorescent markers to measure the distribution of membrane bound tumor markers, for determining enzymatic activity or other biochemical functions, and for monitoring potential test compounds for post-operative cancer treatment, while Walt is asserted to teach fluorescent image scanning of an array of samples in a plurality of microwells. The Applicants traverse the rejection, but have nonetheless amended or canceled the claims to obviate the rejection.

As an initial matter, the applicants note the corrected priority claim made for the present application, which extends to February 27, 1997. The Walt reference's earliest priority claim is March 2, 1998, and thus it is not an effective art reference against the present application.

In order to establish a *prima facie* case of obviousness the patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of one of skill in the art to combine or modify the references; 2) a reasonable expectation of success; and 3) the prior art references alone or in combination must teach or suggest *all* the claim limitations. MPEP § 706.02(j).

Pending claim 13 recites the following:

> 13. (Amended) An automated method for analyzing distribution of a protein of interest between cell membrane and cell cytoplasm comprising:
>
> a) providing an array of locations which contain multiple cells, wherein the cells contain a plurality of fluorescent reporter molecules, wherein the plurality of fluorescent reporter molecules comprise fluorescent reporter molecules that report on cell cytoplasm, fluorescent reporter molecules that report on cell membrane, and fluorescent reporter molecules that report on the protein of interest;

b) automatically imaging multiple cells in each of the locations containing cells to obtain fluorescent signals from the plurality of fluorescent reporter molecules on or in individual cells, wherein the fluorescent signals from the fluorescent reporter molecules that report on cell cytoplasm are used to create cell cytoplasmic masks of individual cells and the fluorescent signals from the fluorescent reporter molecules that report on cell membrane are used to create cell cytoplasmic masks of individual cells;

c) automatically measuring an intensity of the fluorescent signals from the fluorescent reporter molecules that report on the protein of interest in the cell cytoplasmic mask and in the cell membrane mask; and

d) automatically calculating one or both of the following:

i) a ratio of the intensity of the fluorescent signals from the fluorescent reporter molecules that report on the protein of interest in the cell cytoplasmic mask and the cell membrane mask; and

ii) a difference of the intensity of the fluorescent signals from the fluorescent reporter molecules that report on the protein of interest in the cell cytoplasmic mask and the cell membrane mask;

wherein the ratio and/or difference provides a measure of the distribution of the protein of interest between the cytoplasm and the cell membrane in the individual cells.

Morrison does not teach, suggest, or motivate at least the limitations of each of steps (a)-(d) in currently pending claim 13. By way of example, Morrison does not teach, suggest, or motivate: (a) cells containing use of fluorescent reporter molecules that report on each of the cell cytoplasm, the cell membrane, and a protein of interest; (b) creating cell cytoplasm masks and cell membrane masks; (c) measuring fluorescent intensity of the fluorescent signals from the fluorescent reporter molecule that reports on the protein of interest in the cell cytoplasmic and cell membrane masks; or (d) making the calculations recited in step (d). Thus, the Morrison reference is not adequate to support a prima facie case of obviousness of pending claim 13, or its dependent claims. Even if the Walt reference was prior art to the pending application, it does not cure the deficiencies in Morrison, and thus the combination of Walt and Morrison also fails to establish a prima facie case of obviousness. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection.

(b) The patent office rejected claims 21-23 and 27 under 35 USC 103(a) as being obvious over US 5,869,238 ("Morrison") in view of US 6,210,910 ("Walt") and further in

view of US 5,857,786 ("Johnson"). Specifically, the patent office asserts that Morrison teaches using fluorescent markers to measure the distribution of membrane bound tumor markers, for determining enzymatic activity or other biochemical functions, and for monitoring potential test compounds for post-operative cancer treatment, while Walt is asserted to teach fluorescent image scanning of an array of samples in a plurality of microwells and Johnson is asserted to teach analysis of cell cycle proteins. The Applicants traverse the rejection, but have nonetheless amended or canceled the claims to obviate the rejection.

The Morrison and Walt references have been discussed above. The Johnson reference does not cure their deficiencies, as the combination of Morrison, Walt, and Johnson does not teach, suggest, or motivate at least the limitations of each of steps (a)-(d) in currently pending claim 13. By way of example, the combination does not teach, suggest, or motivate: (a) cells containing use of fluorescent reporter molecules that report on each of the cell cytoplasm, the cell membrane, and a protein of interest; (b) creating cell cytoplasm masks and cell membrane masks; (c) measuring fluorescent intensity of the fluorescent signals from the fluorescent reporter molecule that reports on the protein of interest in the cell cytoplasmic and cell membrane masks; or (d) making the calculations recited in step (d).

Thus, the combination of the cited references are not adequate to support a prima facie case of obviousness of pending claim 13, or its dependent claims, and thus the applicants respectfully request reconsideration and withdrawal of the rejection.

(c) The patent office rejected claims 24-25 under 35 USC 103(a) as being obvious over US 5,869,238 ("Morrison") in view of US 6,210,910 ("Walt") and further in view of US 5,857,786 ("Johnson") and further in view of US 6,238,869 ("Kris"). The applicants note the corrected priority claim made for the present application, which extends to February 27, 1997. The Kris reference's earliest priority claim is December 19, 1997, and thus it is not an effective art reference against the present application.

Specifically, the patent office asserts that Morrison teaches using fluorescent markers to measure the distribution of membrane bound tumor markers, for determining enzymatic activity or other biochemical functions, and for monitoring potential test compounds for post-operative cancer treatment, while Walt is asserted to teach fluorescent image scanning of an

array of samples in a plurality of microwells, Johnson is asserted to teach analysis of cell cycle proteins, and Kris is asserted to teach the tyrosin kinase src and its analysis. The Applicants traverse the rejection, but have nonetheless amended or canceled the claims to obviate the rejection.

The Morrison, Walt, and Johnson references have been discussed above. The Kris reference does not cure their deficiencies, as the combination of Morrison, Walt, Johnson, and Kris does not teach, suggest, or motivate at least the limitations of each of steps (a)-(d) in currently pending claim 13. By way of example, the combination does not teach, suggest, or motivate: (a) cells containing use of fluorescent reporter molecules that report on each of the cell cytoplasm, the cell membrane, and a protein of interest; (b) creating cell cytoplasm masks and cell membrane masks; (c) measuring fluorescent intensity of the fluorescent signals from the fluorescent reporter molecule that reports on the protein of interest in the cell cytoplasmic and cell membrane masks; or (d) making the calculations recited in step (d).

Thus, the combination of the cited references are not adequate to support a prima facie case of obviousness of pending claim 13, nor its dependent claims, and thus the applicants respectfully request reconsideration and withdrawal of the rejection.

Based on all of the above, the applicants believe that the application is in condition for allowance. If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned attorney at (312) 913-2106.

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff

Date: 1/4/04

By: _____

David S. Harper
Registration No. 42,636